The Ancient Origins of TRP-dependent Menthol Sensing

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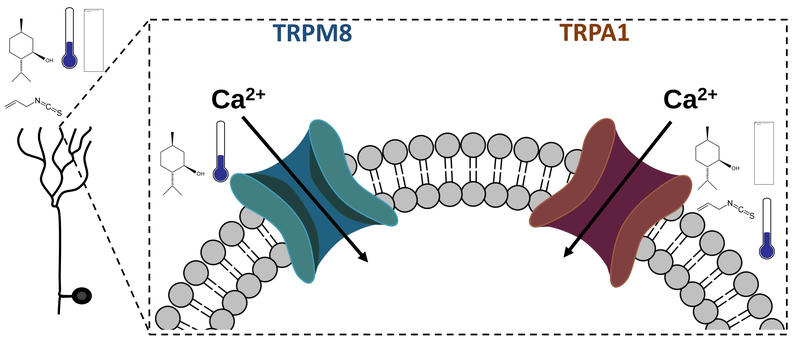
Introduction

Drosophila melanogaster are not big fans of menthol.

Menthol, and other terpenes, affect the behavior of insects, like *Drosophila*

- Menthol affects the behavior of insects like *D. melanogaster.*
- In vertebrates, menthol is sensed by the TRP channels TRPA1 and TRPM8
- However, the mechanisms of menthol sensing in insects remain unknown.

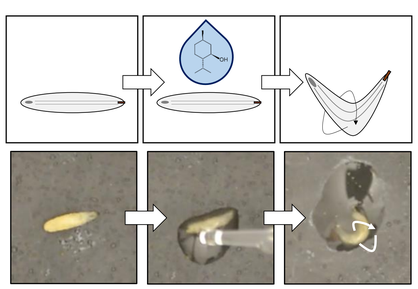
Transient receptor potential (TRP) channels transduce a variety of stimuli, and in mammals, detect menthol

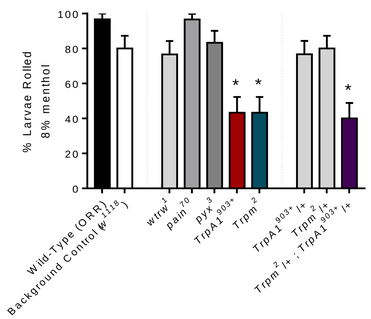


We hypothesized that insect TRP channels play a conserved role in menthol sensing.

Results

Menthol elicits a rolling behavior in *Drosophila melanogaster* larvae



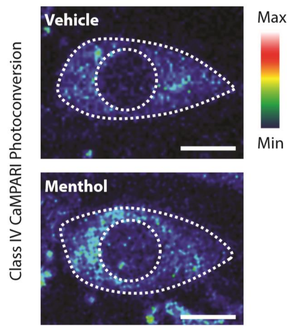


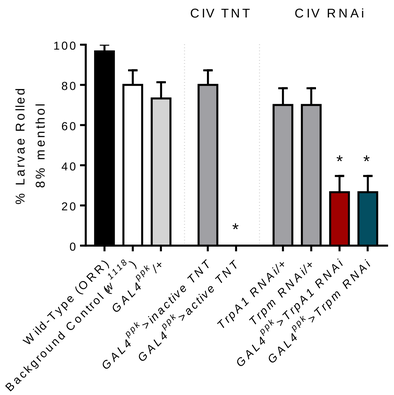
Results

TRP channels function in Class IV (CIV) nociceptors to facilitate menthol-evoked rolling

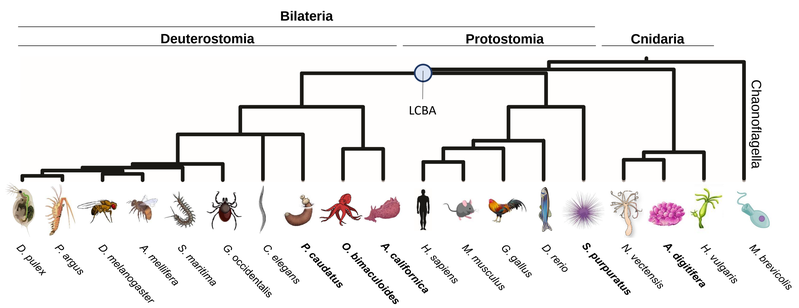
Ca^{2+} imaging shows that CIV neurons are activated by menthol

CIV neurons, and CIV expression of TRP channels, are both required for rolling

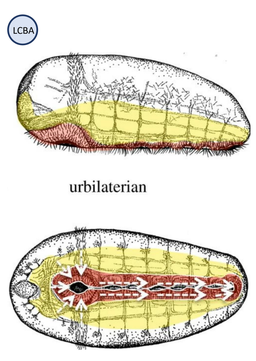




The last common ancestor of *D. melanogaster* and humans existed prior the protostome-deuterostome split (>550mya)



The function of many TRP channels have their origins in or prior to the last common bilaterian ancestor, Urbilateria*



Tosches & Arendt, 2013

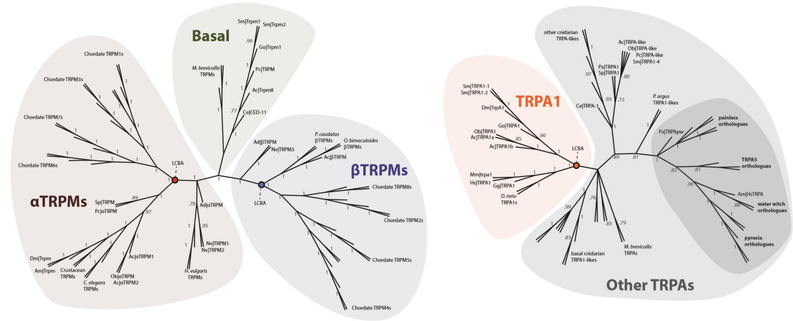
- Some debate over morphology of whole animal & nervous system [7], but likely had some sort of photoreceptive eye spot [8].
- Genome likely encoded a variety of TRP channels, including channels from the TRPM and TRPA subfamilies[9].
- TRPM(s) and TRPA(s) thermal and electrophile sensitivity likely emerged in or prior to urbilaterian [1-3].
- However, it is unknown if the TRP-menthol sensing mechanisms have equally ancient origins.

*These analyses exclude xenacoelomorphs.

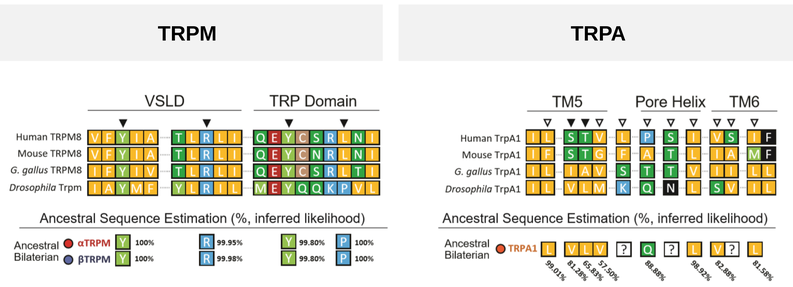
The ancestral nephrozoan genome likely encoded several TRPM/TRPA channels

At least 3 TRPM clades predate the protostome-deuterostome split

TRPA1s predate the protostome-deuterostome split



Many residues critical to menthol sensing emerged prior to the protostome-deuterostome split



Conclusions

These findings, in combination with previous discoveries concerning TRP function, demonstrate that the sensory capacity of TRP channels have origins predating the protostome-deuterostome split (>550mya).

Citations & Acknowledgments

[1]Abed-Vieillard et al., Front Integ Neuro. (2016); [2] Abed-Vieillard et al., Bio Open (2014); [3] Kohno et al., J Neurosci. (2010); [4] Maliszewaska et al., Molecules. (2018); [5] Peier et al., Cell (2002); [6] Karashima et al., J Neurosci. (2007); [7] McKemy et al., Nature (2002); [8] Northcutt, Proc Natl Acad Sci U S A. (2012); [9] Arendt & Wittbrodt, Philos Trans R Soc Lond B Biol Sci. (2001); [10] Peng et al., Mol Phylogenet Evol. (2015); [11] Turner et al., Curr Bio. (2016); [12] Zhong et al., Cell Rep. (2012); [13] Kang et al., Nature (2010); [TRPM8 residues] Rath et al., Curr Bio. (2015); Bandell et al., Nat Neurosci. (2006); [TRPA1 residues] Xiao et al., J Neurosci. (2008); Sequences from publically available databases at FlyBase (*Drosophila*), WormBase (*C. elegans*), JGI (*Nematostella & Daphnia*), CCDS (human & murine), or NCBI (other).

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